=> fil reg; d stat que l9; d ide l9 1-6
FILE 'REGISTRY' ENTERED AT 12:46:54 ON 09 JUL 2003

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 8 JUL 2003 HIGHEST RN 544651-49-2
DICTIONARY FILE UPDATES: 8 JUL 2003 HIGHEST RN 544651-49-2

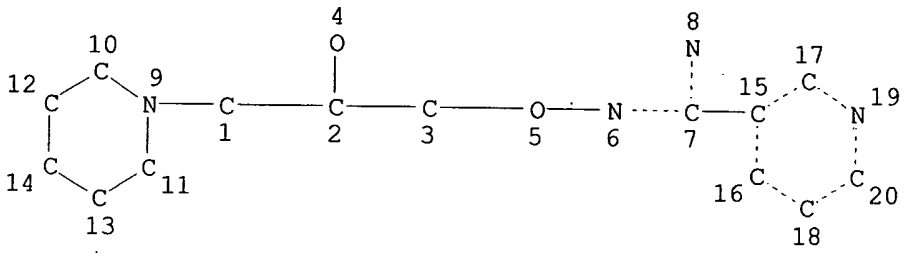
TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

L7 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

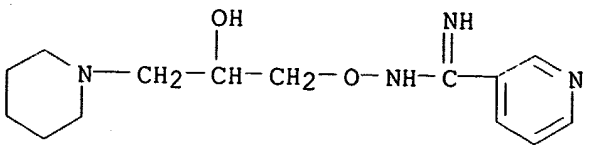
GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 20

STEREO ATTRIBUTES: NONE
L9 6 SEA FILE=REGISTRY FAM FUL L7

100.0% PROCESSED 66 ITERATIONS 6 ANSWERS
SEARCH TIME: 00.00.01

L9 ANSWER 1 OF 6 REGISTRY COPYRIGHT 2003 ACS
RN 459809-32-6 REGISTRY
CN 3-Pyridinecarboximidamide, N-[2-hydroxy-3-(1-piperidinyl)propoxy]-, monohydrochloride (9CI) (CA INDEX NAME)
OTHER NAMES:
CN BGP 15M
MF C14 H22 N4 O2 . Cl H
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

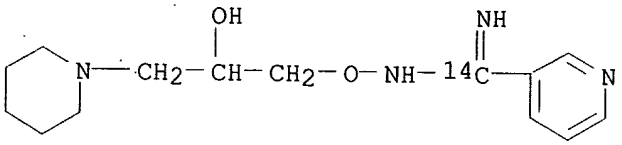
CRN (66611-38-9)



● HCl

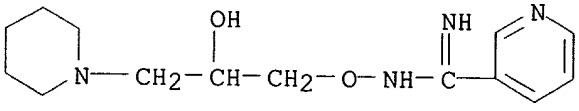
2 REFERENCES IN FILE CA (1957 TO DATE)
2 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L9 ANSWER 2 OF 6 REGISTRY COPYRIGHT 2003 ACS
RN 170693-20-6 REGISTRY
CN 3-Pyridinecarboximidamide-14C, N-[2-hydroxy-3-(1-piperidinyl)propoxy]-(9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C14 H22 N4 O2
SR CA
LC STN Files: CA, CAPLUS



2 REFERENCES IN FILE CA (1957 TO DATE)
2 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L9 ANSWER 3 OF 6 REGISTRY COPYRIGHT 2003 ACS
RN 131782-72-4 REGISTRY
CN 3-Pyridinecarboximidamide, N-[2-hydroxy-3-(1-piperidinyl)propoxy]-, dihydrobromide (9CI) (CA INDEX NAME)
MF C14 H22 N4 O2 . 2 Br H
SR CA
LC STN Files: CA, CAPLUS, DRUGUPDATES, USPATFULL
CRN (66611-38-9)



●2 HBr

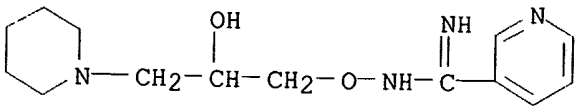
1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L9 ANSWER 4 OF 6 REGISTRY COPYRIGHT 2003 ACS
RN 66611-39-0 REGISTRY
CN 3-Pyridinecarboxylic acid, compd. with N-[2-hydroxy-3-(1-

piperidinyl)propoxy]-3-pyridinecarboximidamide (1:1) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 3-Pyridinecarboximidamide, N-[2-hydroxy-3-(1-piperidinyl)propoxy]-, mono-3-pyridinecarboxylate (salt) (9CI)
MF C14 H22 N4 O2 . C6 H5 N O2
LC STN Files: CA, CAPLUS, DRUGUPDATES, USPATFULL

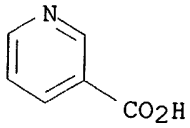
CM 1

CRN 66611-38-9
CMF C14 H22 N4 O2



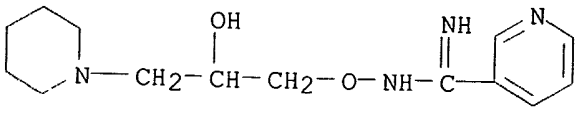
CM 2

CRN 59-67-6
CMF C6 H5 N O2



1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

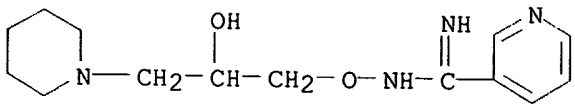
L9 ANSWER 5 OF 6 REGISTRY COPYRIGHT 2003 ACS
RN 66611-38-9 REGISTRY
CN 3-Pyridinecarboximidamide, N-[2-hydroxy-3-(1-piperidinyl)propoxy]- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN NP 51
FS 3D CONCORD
DR 79104-68-0
MF C14 H22 N4 O2
CI COM
LC STN Files: BEILSTEIN*, CA, CAPLUS, DRUGUPDATES, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

15 REFERENCES IN FILE CA (1957 TO DATE)
15 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L9 ANSWER 6 OF 6 REGISTRY COPYRIGHT 2003 ACS
RN 66611-37-8 REGISTRY
CN 3-Pyridinecarboximidamide, N-[2-hydroxy-3-(1-piperidinyl)propoxy]-, dihydrochloride (9CI) (CA INDEX NAME)
OTHER NAMES:
CN BGP 15
MF C14 H22 N4 O2 . 2 Cl H
LC STN Files: BIOSIS, CA, CAPLUS, CIN, DRUGUPDATES, PROMT, SYNTHLINE, TOXCENTER, USPATFULL
CRN (66611-38-9)



●2 HCl

11 REFERENCES IN FILE CA (1957 TO DATE)
11 REFERENCES IN FILE CAPLUS (1957 TO DATE)

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=> fil hcapl; d que nos 119; fil toxcenter;d que nos 134; fil uspatf; d que nos 149
FILE 'HCAPLUS' ENTERED AT 13:12:42 ON 09 JUL 2003
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FILE COVERS 1907 - 9 Jul 2003  VOL 139 ISS 2
FILE LAST UPDATED: 8 Jul 2003  (20030708/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L7              STR
L9            6 SEA FILE=REGISTRY FAM FUL L7
L10          72 SEA FILE=HCAPLUS ABB=ON  SUMEGI B?/AU
L11          23 SEA FILE=HCAPLUS ABB=ON  L9
L12      275914 SEA FILE=HCAPLUS ABB=ON  ANTITUMOR AGENTS+OLD,NT,RTCS/CT
L13       13187 SEA FILE=HCAPLUS ABB=ON  CYTOPROTECTIVE AGENTS/CT
L14       27858 SEA FILE=HCAPLUS ABB=ON  DRUG INTERACTIONS+OLD,NT/CT
L15       67891 SEA FILE=HCAPLUS ABB=ON  TOXICITY+NT/CT
L16       10083 SEA FILE=HCAPLUS ABB=ON  CYTOTOXICITY+OLD/CT
L17       14612 SEA FILE=HCAPLUS ABB=ON  (SIDE OR ADVERSE)(L)(EFFECT# OR
                EVENT# OR REACTION#)/OBI
L19           7 SEA FILE=HCAPLUS ABB=ON  L10 AND L11 AND (L12 OR L13 OR L14 OR
                L15 OR L16 OR L17)


FILE 'TOXCENTER' ENTERED AT 13:12:42 ON 09 JUL 2003
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FILE COVERS 1907 TO 8 Jul 2003 (20030708/ED)

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TOXCENTER has been enhanced with new files segments and search fields.
See HELP CONTENT for more information.

TOXCENTER thesauri in the /CN, /CT, and /MN fields incorporate the
MeSH 2003 vocabulary.  See http://www.nlm.nih.gov/mesh/summ[illegible].html
for a description on changes.
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L7              STR
L9            6 SEA FILE=REGISTRY FAM FUL L7
L32           8 SEA FILE=TOXCENTER ABB=ON  L9
L33          32 SEA FILE=TOXCENTER ABB=ON  SUMEGI B?/AU
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L34 7 SEA FILE=TOXCENTER ABB=ON L32 AND L33

FILE 'USPATFULL' ENTERED AT 13:12:42 ON 09 JUL 2003
CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 8 Jul 2003 (20030708/PD)
FILE LAST UPDATED: 8 Jul 2003 (20030708/ED)
HIGHEST GRANTED PATENT NUMBER: US6591423
HIGHEST APPLICATION PUBLICATION NUMBER: US2003126664
CA INDEXING IS CURRENT THROUGH 8 Jul 2003 (20030708/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 8 Jul 2003 (20030708/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2003
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2003

>>> USPAT2 is now available. USPATFULL contains full text of the <<<
>>> original, i.e., the earliest published granted patents or <<<
>>> applications. USPAT2 contains full text of the latest US <<<
>>> publications, starting in 2001, for the inventions covered in <<<
>>> USPATFULL. A USPATFULL record contains not only the original <<<
>>> published document but also a list of any subsequent <<<
>>> publications. The publication number, patent kind code, and <<<
>>> publication date for all the US publications for an invention <<<
>>> are displayed in the PI (Patent Information) field of USPATFULL <<<
>>> records and may be searched in standard search fields, e.g., /PN, <<<
>>> /PK, etc. <<<

>>> USPATFULL and USPAT2 can be accessed and searched together <<<
>>> through the new cluster USPATALL. Type FILE USPATALL to <<<
>>> enter this cluster. <<<
>>> <<<
>>> Use USPATALL when searching terms such as patent assignees, <<<
>>> classifications, or claims, that may potentially change from <<<
>>> the earliest to the latest publication. <<<

This file contains CAS Registry Numbers for easy and accurate substance identification.

L7 STR
L9 6 SEA FILE=REGISTRY FAM FUL L7
L40 15 SEA FILE=USPATFULL ABB=ON L9
L41 7 SEA FILE=USPATFULL ABB=ON SUMEGI B?/AU
L49 5 SEA FILE=USPATFULL ABB=ON L40 AND L41

=> dup rem l19,l34,l49

FILE 'HCAPLUS' ENTERED AT 13:12:43 ON 09 JUL 2003
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FILE 'TOXCENTER' ENTERED AT 13:12:43 ON 09 JUL 2003
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FILE 'USPATFULL' ENTERED AT 13:12:43 ON 09 JUL 2003
CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)
PROCESSING COMPLETED FOR L19
PROCESSING COMPLETED FOR L34
PROCESSING COMPLETED FOR L49
L58 14 DUP REM L19 L34 L49 (5 DUPLICATES REMOVED)

ANSWERS '1-7' FROM FILE HCAPLUS
ANSWERS '8-9' FROM FILE TOXCENTER
ANSWERS '10-14' FROM FILE USPATFULL

=>

=> d ibib ab hitrn 1-14

L58 ANSWER 1 OF 14 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 1
ACCESSION NUMBER: 2002:251444 HCAPLUS
DOCUMENT NUMBER: 137:332798
TITLE: BGP-15 - a novel poly(ADP-ribose) polymerase inhibitor - protects against nephrotoxicity of cisplatin without compromising its antitumor activity
AUTHOR(S): Racz, Ildiko; Tory, Kalman; Gallyas, Ferenc; Berente, Zoltan; Osz, Erzsebet; Jaszlits, Laszlo; Bernath, Sandor; **Sumegi, Balazs**; Rabloczky, Gyorgy; Literati-Nagy, Peter
CORPORATE SOURCE: N-Gene R&D, Budapest, Hung.
SOURCE: Biochemical Pharmacology (2002), 63(6), 1099-1111
CODEN: BCPCA6; ISSN: 0006-2952
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Nephrotoxicity is 1 of the major dose limiting side effects of cisplatin chemotherapy. The antitumor and toxic effects are mediated in part by different mechanisms, thus, permitting a selective inhibition of certain side effects. The influence of O-(3-piperidino-2-hydroxy-1-propyl)nicotinic amidoxime (BGP-15) - a poly(ADP-ribose) polymerase (PARP) inhibitor - on the nephrotoxicity and antitumor efficacy of cisplatin was evaluated in exptl. models. BGP-15 either blocked or significantly reduced (60-90% in 100-200 mg/kg oral dose) cisplatin induced increase in blood serum urea and creatinine level in mice and rats and prevented the structural degeneration of the kidney, as well. The nephroprotective effect of BGP-15 treatment was revealed also in living mice by MRI anal. manifesting in the lack of edema which otherwise developed as a result of cisplatin treatment. The protective effect was accompanied by inhibition of cisplatin-induced poly-ADP-ribosylation and by the restoration of the disturbed energy metab. The preservation of ATP level in the kidney was demonstrated in vivo by localized NMR spectroscopy. BGP-15 decreased cisplatin-induced ROS prodn. in rat kidney mitochondria and improved the antioxidant status of the kidney in mice with cisplatin-induced nephropathy. In rat kidney, cisplatin caused a decrease in the level of Bcl-x, a mitochondrial protective protein, and this was normalized by BGP-15 treatment. On the other hand, BGP-15 did not inhibit the antitumor efficacy of cisplatin in cell culture and in transplantable solid tumors of mice. Treatment with BGP-15 increased the mean survival time of cisplatin-treated P-388 leukemia bearing mice from 13 to 19 days. PARP inhibitors were demonstrated to diminish the consequences of free radical-induced damage, and this is related to the chemoprotective effect of BGP-15, a novel PARP inhibitor. Based on these results, the authors propose that BGP-15 represents a novel, non-thiol chemoprotective agent.

IT **15663-27-1**, Cisplatin
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(BGP-15 protects against cisplatin-induced nephrotoxicity)

IT **66611-37-8**, BGP 15
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(BGP-15 protects against cisplatin-induced nephrotoxicity)

IT **9055-67-8**, Poly(ADP-ribose) polymerase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor; BGP-15 protects against cisplatin-induced nephrotoxicity)

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 2 OF 14 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 2
ACCESSION NUMBER: 2002:211608 HCAPLUS
DOCUMENT NUMBER: 137:306693
TITLE: Reduction of acute photodamage in skin by topical application of a novel PARP inhibitor
AUTHOR(S): Farkas, Beatrix; Magyarlaki, Marta; Csete, Bela; Nemeth, Jozsef; Rabloczky, Gyorgy; Bernath, Sandor; Literati Nagy, Peter; **Sumegi, Balazs**
CORPORATE SOURCE: Faculty of Medicine, Department of Dermatology, University of Pecs, Pecs, H-7624, Hung.
SOURCE: Biochemical Pharmacology (2002), 63(5), 921-932
CODEN: BCPCA6; ISSN: 0006-2952
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The UV components of sunlight induce damage to the DNA in skin cells, which is considered to be the initiating step in the harmful biol. effects of UV radiation. Repair of DNA damage results in the formation of single-strand DNA breaks, which activate the nuclear poly(ADP-ribose) polymerase (PARP). Overactivation of PARP worsens the oxidative cell damage and impairs the energy metab., raising the possibility that moderation of PARP activation following DNA damage may protect skin cells from UV radiation. The topical effects of the novel PARP inhibitor O-(3-piperidino-2-hydroxy-1-propyl) pyridine-3-carboxylic acid amidoxime monohydrochloride (BGP-15M) were investigated on UV-induced skin damage in a hairless mouse model. For evaluation of the UV-induced acute photodamage to the skin and the potential protective effect of BGP-15M, DNA injury was detected by measuring the formation of single-strand DNA breaks and counting the resulting sunburn (apoptotic) cells. The ADP-ribosylation of PARP was assessed by Western blot anal. and then quantified. In addn., the UV-induced immunosuppression was investigated by the immunostaining of tumor necrosis factor alpha and interleukin-10 expressions in epidermal cells. The signs of inflammation were examd. clin. and histochem. Besides its primary effect in decreasing the activity of nuclear PARP, topically applied BGP-15M proved to be protective against solar and artificial UV radiation-induced acute skin damage. The DNA injury was decreased ($P<0.01$). An inhibition of immunosuppression was obsd. by down-regulation of the epidermal prodn. of cytokines IL-10 and TNF.alpha.. In the mouse skin, clin. or histol. signs of UV-induced inflammation could not be obsd. These data suggest that BGP-15M directly interferes with UV-induced cellular processes and modifies the activity of PARP. The effects provided by topical application of the new PARP-regulator BGP-15M indicate that it may be a novel type of agent in photoprotection of the skin.

IT **9055-67-8**, Poly(ADP-ribose) polymerase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(redn. of acute photodamage in skin by topical application of PARP inhibitor)

IT **66611-37-8**, BGP 15 **66611-38-9** **459809-32-6**, BGP 15M
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(redn. of acute photodamage in skin by topical application of PARP inhibitor)

REFERENCE COUNT: 79 THERE ARE 79 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 3 OF 14 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 3
ACCESSION NUMBER: 2001:402235 HCAPLUS
DOCUMENT NUMBER: 135:221029

TITLE: Effect of poly(ADP-ribose) polymerase inhibitors on the ischemia-reperfusion-induced oxidative cell damage and mitochondrial metabolism in Langendorff heart perfusion system

AUTHOR(S): Halmosi, Robert; Berente, Zoltan; Osz, Erzsebet; Toth, Kalman; Literati-Nagy, Peter; **Sumegi, Balazs**

CORPORATE SOURCE: Departments of Biochemistry, Faculty of Medicine, University of Pecs, Pecs, Hung.

SOURCE: Molecular Pharmacology (2001), 59(6), 1497-1505
CODEN: MOPMA3; ISSN: 0026-895X

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Ischemia-reperfusion induces reactive oxygen species (ROS) formation, and ROS lead to cardiac dysfunction, in part, via the activation of the nuclear poly(ADP-ribose) polymerase (PARP, called also PARS and ADP-RT). ROS and peroxynitrite induce single-strand DNA break formation and PARP activation, resulting in NAD+ and ATP depletion, which can lead to cell death. Although protection of cardiac muscle by PARP inhibitors can be explained by their attenuating effect on NAD+ and ATP depletion, there are data indicating that PARP inhibitors also protect mitochondria from oxidant-induced injury. Studying cardiac energy metab. in Langendorff heart perfusion system by 31P NMR, the authors found that PARP inhibitors (3-aminobenzamide, nicotinamide, BGP-15, and 4-hydroxyquinazoline) improved the recovery of high-energy phosphates (ATP, creatine phosphate) and accelerated the reutilization of inorg. phosphate formed during the ischemic period, showing that PARP inhibitors facilitate the faster and more complete recovery of the energy prodn. Furthermore, PARP inhibitors significantly decrease the ischemia-reperfusion-induced increase of lipid peroxidn., protein oxidn., single-strand DNA breaks, and the inactivation of respiratory complexes, which indicate a decreased mitochondrial ROS prodn. in the reperfusion period. Surprisingly, PARP inhibitors, but not the chem. similar 3-aminobenzoic acid, prevented the H2O2-induced inactivation of cytochrome oxidase in isolated heart mitochondria, suggesting the presence of an addnl. mitochondrial target for PARP inhibitors. Therefore, PARP inhibitors, in addn. to their important primary effect of decreasing the activity of nuclear PARP and decreasing NAD+ and ATP consumption, reduce ischemia-reperfusion-induced endogenous ROS prodn. and protect the respiratory complexes from ROS induced inactivation, providing an addnl. mechanism by which they can protect heart from oxidative damages.

IT **66611-37-8**, BGP 15
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of poly(ADP-ribose) polymerase inhibitors on ischemia-reperfusion-induced oxidative cell damage and mitochondrial metab. in Langendorff heart perfusion system in relation to cardioprotective effective)

IT **9055-67-8**, poly(ADP-ribose) polymerase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(effect of poly(ADP-ribose) polymerase inhibitors on ischemia-reperfusion-induced oxidative cell damage and mitochondrial metab. in Langendorff heart perfusion system in relation to cardioprotective effective)

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 4 OF 14 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 4
ACCESSION NUMBER: 2000:517271 HCAPLUS
DOCUMENT NUMBER: 133:358726
TITLE: Protective effect of poly(ADP-ribose) polymerase

Searched by Barb O'Bryen, STIC 308-4291

inhibitors against cell damage induced by antiviral and anticancer drugs

AUTHOR(S): **Sumegi, Balazs**; Rabloczky, Gyorgy; Racz, Ildiko; Tory, Kalman; Bernath, Sandor; Varbiro, Gabor; Gallyas, Ferenc, Jr.; Nagy, Peter Literati

CORPORATE SOURCE: Department of Biochemistry, University Medical School Pecs, Pecs, Hung.

SOURCE: Cell Death (2000), 167-182. Editor(s): Szabo, Csaba. CRC Press LLC: Boca Raton, Fla.
CODEN: 69AEOT

DOCUMENT TYPE: Conference; General Review
LANGUAGE: English

AB A review with 78 refs. including the authors own work is given on the role of poly(ADP-ribose) polymerase (PARP) activation in the cytotoxicity of deoxynucleoside analogs and dideoxynucleoside antiviral drugs, and reactive oxygen species (ROS)-mediated cytotoxicity of antitumor drugs. BGP-15, a novel PARP inhibitor, was used in combination with 3'-azido-3'-deoxythymidine (AZT) to investigate whether PARP inhibitors can protect the heart from AZT-induced cardiac damages in rats. AZT treatment for 2 wk increased the RR, PR, and QT intervals, and caused a change in J point depressions in leads I and aVL that correspond to the main muscle mass of the left ventricle. Heart abnormalities were much lighter in the treatment group with AZT and BGP-15, and BGP-15 protected rat hearts from AZT-induced decreases in the activity of the respiratory complexes. It was investigated whether BGP-15 can decrease the mortality caused by cisplatin treatment in mice. Cisplatin alone caused 67% mortality while BPG-15 reduced the mortality rate to 40%. Cisplatin treatment caused an increase in blood serum urea levels. In combination with BGP-15 or amifostine, urea levels remained close to control levels.

IT **66611-37-8**, BGP 15
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(BGP 15; protective effect of poly(ADP-ribose) polymerase inhibitors against cell damage)

IT **15663-27-1**, Cisplatin
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protective effect of poly(ADP-ribose) polymerase inhibitors against cell damage)

IT **9055-67-8**, Poly(ADP-ribose) polymerase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(protective effect of poly(ADP-ribose) polymerase inhibitors against cell damage)

REFERENCE COUNT: 78 THERE ARE 78 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 5 OF 14 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 5
ACCESSION NUMBER: 1999:27740 HCAPLUS
DOCUMENT NUMBER: 130:90498
TITLE: Pharmaceutical composition having enhanced antitumor activity and/or reduced **side effects**, containing an antitumor agent and an hydroxamic acid derivative
INVENTOR(S): **Sumegi, Balazs**
PATENT ASSIGNEE(S): N-Gene Research Laboratories Inc., USA
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9858676	A1	19981230	WO 1998-IB961	19980622
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9877837	A1	19990104	AU 1998-77837	19980622
AU 735922	B2	20010719		
EP 993304	A1	20000419	EP 1998-925873	19980622
EP 993304	B1	20030402		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9810312	A	20000919	BR 1998-10312	19980622
JP 2002508762	T2	20020319	JP 1999-504049	19980622
NZ 502039	A	20020328	NZ 1998-502039	19980622
AT 235918	E	20030415	AT 1998-925873	19980622
MX 9911656	A	20000930	MX 1999-11656	19991214
NO 9906349	A	20000223	NO 1999-6349	19991220
US 6440998	B1	20020827	US 2000-446064	20000217
US 2002147213	A1	20021010	US 2002-84183	20020228
US 2003050345	A1	20030313	US 2002-84095	20020228
US 2003069270	A1	20030410	US 2002-106227	20020327

PRIORITY APPLN. INFO.: HU 1997-1081 A 19970623
WO 1998-IB961 W 19980622
US 2000-446064 A3 20000217

OTHER SOURCE(S): MARPAT 130:90498

AB Pharmaceutical compns. are provided which have an enhanced antitumor activity or reduced side effect(s), comprising a known active substance having antitumor effect, or a pharmaceutically acceptable salt thereof, and a hydroximic acid deriv. (Markush included) or a therapeutically useful acid addn. salt thereof. The hydroximic acid deriv. is e.g. O-(3-piperidino-2-hydroxy-1-propyl)nicotinic amidoxime.

IT **51-21-8**, Fluorouracil **15663-27-1**, Cisplatin
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydroximic acid deriv.-antitumor agent pharmaceutical compn. with enhanced antitumor activity and/or reduced **side effects**)

IT **66611-37-8 66611-38-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydroximic acid deriv.-antitumor agent pharmaceutical compn. with enhanced antitumor activity and/or reduced **side effects**)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 6 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:116885 HCAPLUS
DOCUMENT NUMBER: 132:161247
TITLE: Pharmaceutical compositions containing hydroximic acids for the treatment of autoimmune diseases
INVENTOR(S): **Sumegi, Balazs**
PATENT ASSIGNEE(S): N-Gene Kutato Kft., Hung.
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2

Searched by Barb O'Bryen, STIC 308-4291

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000007580	A2	20000217	WO 1999-HU54	19990802
WO 2000007580	A3	20000518		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9952967	A1	20000228	AU 1999-52967	19990802

PRIORITY APPLN. INFO.:

HU 1998-1772	A	19980803
HU 1999-2398	A	19990719
WO 1999-HU54	W	19990802

OTHER SOURCE(S): MARPAT 132:161247

AB Hydroximic acid derivs. R3AC(X)(B)N(R)OCH2CH(Y)CH2N(R1)(R2) [R1 = H, C1-5 alkyl; R2 = H, C1-5 alkyl, C3-8 cycloalkyl, (substituted) Ph, or R1NR2 form 5-8-membered ring optionally contg. other heteroatoms and condensed with another ring; R3 = H, (substituted) Ph, (substituted) naphthyl, (substituted) pyridyl; Y = H, OH, (amino-substituted) C1-24 alkoxy, etc.; X = halo, amino, C1-4 alkoxy, or X forms with B an O, or X and Y form ring; R = H or R and B form chem. bond; A = C1-4 alkylene, bond, etc.] are used for the prepn. of a pharmaceutical compn. to treat autoimmune diseases.

IT **66611-38-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydroximic acids for treatment of autoimmune diseases)

IT **9055-67-8**, Poly(ADP-ribose)polymerase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(hydroximic acids for treatment of autoimmune diseases)

L58 ANSWER 7 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:127294 HCAPLUS
DOCUMENT NUMBER: 132:329682
TITLE: BGP-15, a nicotinic amidoxime derivate protecting heart from ischemia reperfusion injury through modulation of poly(ADP-ribose) polymerase
AUTHOR(S): Szabados, E.; Literati-Nagy, P.; Farkas, B.; **Sumegi, B.**
CORPORATE SOURCE: Department of Biochemistry, University Medical School Pecs, Pecs, Hung.
SOURCE: Biochemical Pharmacology (2000), 59(8), 937-945
CODEN: BCPCA6; ISSN: 0006-2952
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The protective effect of O-(3-piperidino-2-hydroxy-1-propyl)nicotinic amidoxime (BGP-15) against ischemia-reperfusion-induced injury was studied in the Langendorff heart perfusion system. To understand the mol. mechanism of the cardioprotection, the effect of BGP-15 on ischemic-reperfusion-induced reactive oxygen species (ROS) formation, lipid peroxidn. single-strand DNA break formation, NAD+ catabolism, and

endogenous ADP-ribosylation reactions were investigated. These studies showed that BGP-15 significantly decreased leakage of lactate dehydrogenase, creatine kinase, and aspartate aminotransferase in reperfused hearts, and reduced the rate of NAD+ catabolism. In addn., BGP-15 dramatically decreased the ischemia-reperfusion-induced self-ADP-ribosylation of nuclear poly(ADP-ribose) polymerase (PARP) and the mono-ADP-ribosylation of an endoplasmic reticulum chaperone GRP78. These data raise the possibility that BGP-15 may have a direct inhibitory effect on PARP. This hypothesis was tested on isolated enzyme, and kinetic anal. showed a mixed-type (noncompetitive) inhibition with a Ki = 57.+-.6 .mu.M. Furthermore, BGP-15 decreased levels of ROS, lipid peroxidn., and single-strand DNA breaks in reperfused hearts. These data suggest that PARP may be an important mol. target of BGP-15 and that BGP-15 decreases ROS levels and cell injury during ischemia-reperfusion in the heart by inhibiting PARP activity.

IT **66611-37-8**, BGP 15
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(BGP-15, a nicotinic amidoxime derivate protecting heart from ischemia reperfusion injury through modulation of poly(ADP-ribose) polymerase)

IT **9055-67-8**, Poly(ADP-ribose) polymerase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(BGP-15, a nicotinic amidoxime derivate protecting heart from ischemia reperfusion injury through modulation of poly(ADP-ribose) polymerase)

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 8 OF 14 TOXCENTER COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:177803 TOXCENTER
COPYRIGHT: Copyright 2003 BIOSIS
DOCUMENT NUMBER: PREV200100470884
TITLE: Mode of action observations of a new chemoprotective agent BGP-15
AUTHOR(S): Tory, Kalman (1); Racz, Ildiko; Gallyas, Ferenc; Jaszlits, Laszlo; Bernath, Sandor; **Sumegi, Balazs**; Rabloczky, Gyorgy; Literati-Nagy, Peter
CORPORATE SOURCE: (1) Department of Biochemistry, University of Pecs, Faculty of Medicine Pecs, Pecs Hungary
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2001) Vol. 42, pp. 512. print.
Meeting Info.: 92nd Annual Meeting of the American Association for Cancer Research New Orleans, LA, USA March 24-28, 2001
ISSN: 0197-016X.
DOCUMENT TYPE: Conference
FILE SEGMENT: BIOSIS
OTHER SOURCE: BIOSIS 2001:470884
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20020226

L58 ANSWER 9 OF 14 TOXCENTER COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:100428 TOXCENTER
COPYRIGHT: Copyright 2003 BIOSIS
DOCUMENT NUMBER: PREV200000529158
TITLE: Inhibition of nuclear poly(ADP-ribose) polymerase protects the kidney from cytotoxic damage
AUTHOR(S): Racs, I. B. (1); Tory, K. (1); Jaszlits, L. (1); Rabloczky, G. (1); Bernath, S. (1); **Sumegi, B.**;

Literati-Nagy, P. (1)
CORPORATE SOURCE: (1) N-Gene R and D, Budapest Hungary
SOURCE: Journal of Physiology (Cambridge), (August, 2000) Vol. 526P, pp. 178P-179P. print.
Meeting Info.: Scientific Meeting of the Physiological Society Budapest, Hungary May 27-29, 2000 Physiological Society.
ISSN: 0022-3751.
DOCUMENT TYPE: Conference
~~FILE SEGMENT: BIOSIS~~
OTHER SOURCE: BIOSIS 2000:529158
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20020115

L58 ANSWER 10 OF 14 USPATFULL
ACCESSION NUMBER: 2003:100159 USPATFULL
TITLE: Pharmaceutical composition having enhanced antitumor activity and/or reduced side effects, containing an antitumor agent and an hydroxImic acid derivative
INVENTOR(S): **Sumegi, Balazs**, Pecs, HUNGARY
PATENT ASSIGNEE(S): N-Gene Research Laboratories, Inc. (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003069270	A1	20030410
APPLICATION INFO.:	US 2002-106227	A1	20020327 (10)

RELATED APPLN. INFO.: Division of Ser. No. US 2000-446064, filed on 17 Feb 2000, GRANTED, Pat. No. US 6440998 A 371 of International Ser. No. WO 1998-IB961, filed on 22 Jun 1998, UNKNOWN

	NUMBER	DATE
PRIORITY INFORMATION:	HU 1997-P1081	19970623

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BIRCH STEWART KOLASCH & BIRCH, PO BOX 747, FALLS CHURCH, VA, 22040-0747
NUMBER OF CLAIMS: 4
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 3 Drawing Page(s)
LINE COUNT: 804
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention refers to pharmaceutical compositions which have an enhanced antitumor activity or reduced side effect(s) comprising a known active substance having antitumor effect or a pharmaceutically acceptable salt thereof and a hydroximic acid derivative of formula (I) or a therapeutically useful acid addition salt thereof.
IT **66611-37-8 66611-38-9**
(hydroximic acid deriv.-antitumor agent pharmaceutical compn. with enhanced antitumor activity and/or reduced side effects)

L58 ANSWER 11 OF 14 USPATFULL
ACCESSION NUMBER: 2003:72058 USPATFULL
TITLE: Pharmaceutical composition having enhanced antitumor activity and/or reduced side effects, containing an antitumor agent and an hydroximic acid derivative
INVENTOR(S): **Sumegi, Balazs**, Pecs, HUNGARY
PATENT ASSIGNEE(S): N-Gene Research Laboratories, Inc. (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003050345	A1	20030313
APPLICATION INFO.:	US 2002-84095	A1	20020228 (10)
RELATED APPLN. INFO.:	Division of Ser. No. US 2000-446064, filed on 17 Feb 2000, PENDING A 371 of International Ser. No. WO 1998-IB961, filed on 22 Jun 1998, UNKNOWN		

	NUMBER	DATE
PRIORITY INFORMATION:	HU 1997-P1081	19970623
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	BIRCH STEWART KOLASCH & BIRCH, PO BOX 747, FALLS CHURCH, VA, 22040-0747	
NUMBER OF CLAIMS:	10	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	3 Drawing Page(s)	
LINE COUNT:	815	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention refers to pharmaceutical compositions which have an enhanced antitumor activity or reduced side effect(s) comprising a known active substance having antitumor effect or a pharmaceutically acceptable salt thereof and a hydroximic acid derivative of formula (I) or a therapeutically useful acid addition salt thereof.

IT **66611-37-8 66611-38-9**
(hydroximic acid deriv.-antitumor agent pharmaceutical compn. with enhanced antitumor activity and/or reduced side effects)

L58 ANSWER 12 OF 14 USPATFULL

ACCESSION NUMBER:	2002:266334 USPATFULL
TITLE:	Pharmaceutical composition having enhanced antitumor activity and/or reduced side effects, containing an antitumor agent and an hydroximic acid derivative
INVENTOR(S):	**Sumegi, Balazs**, Pecs, HUNGARY
PATENT ASSIGNEE(S):	N-Gene Research Laboratories, Inc. (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002147213	A1	20021010
APPLICATION INFO.:	US 2002-84183	A1	20020228 (10)
RELATED APPLN. INFO.:	Division of Ser. No. US 2000-446064, filed on 17 Feb 2000, PENDING A 371 of International Ser. No. WO 1998-IB961, filed on 22 Jun 1998, UNKNOWN		

	NUMBER	DATE
PRIORITY INFORMATION:	HU 1997-P1081	19970623
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	BIRCH STEWART KOLASCH & BIRCH, PO BOX 747, FALLS CHURCH, VA, 22040-0747	
NUMBER OF CLAIMS:	12	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	3 Drawing Page(s)	
LINE COUNT:	845	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB ##STR1##

The invention refers to pharmaceutical compositions which have an enhanced antitumor activity or reduced side effect(s) comprising a known

active substance having antitumor effect or a pharmaceutically acceptable salt thereof and a hydroximic acid derivative of formula (I) or a therapeutically useful acid addition salt thereof.

IT **66611-37-8 66611-38-9**
(hydroximic acid deriv.-antitumor agent pharmaceutical compn. with enhanced antitumor activity and/or reduced side effects)

L58 ANSWER 13 OF 14 USPATFULL
ACCESSION NUMBER: 2002:239055 USPATFULL
TITLE: Pharmaceutical composition with antiviral activity containing an hydroxymic acid derivative and an antiviral agent
INVENTOR(S): **Sumegi, Balazs**, Pecs, HUNGARY
PATENT ASSIGNEE(S): N-Gene Research Laboratories Inc., New York, NY, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6451851	B1	20020917	
	WO 9858675		19981230	
APPLICATION INFO.:	US 2000-446650		20000323	(9)
	WO 1998-IB960		19980622	
			20000323	PCT 371 date

	NUMBER	DATE
PRIORITY INFORMATION:	HU 1997-1080	19970623

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Travers, Russell
LEGAL REPRESENTATIVE: Birch Stewart Kolasch & Birch LLP
NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 367
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention refers to pharmaceutical compositions having an enhanced antiviral activity and/or decreased side effects. The composition comprises a hydroximic acid derivative of formula (I), or a therapeutically useful acid addition salt thereof and a known antiviral agent or, if desired, a therapeutically useful acid addition or therapeutically useful salt thereof. ##STR1##

IT **66611-38-9**
(synergistic antiviral compn. contg. hydroxamic acid deriv. and antiviral agent)

L58 ANSWER 14 OF 14 USPATFULL
ACCESSION NUMBER: 2002:217283 USPATFULL
TITLE: Pharmaceutical composition having enhanced antitumor activity and/or reduced side effects, containing an antitumor agent and an hydroximic acid derivative
INVENTOR(S): **Sumegi, Balazs**, Pecs, HUNGARY
PATENT ASSIGNEE(S): N-Gene Research Laboratories, Inc., New York, NY, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6440998	B1	20020827	
	WO 9858676		19981230	
APPLICATION INFO.:	US 2000-446064		20000217	(9)
	WO 1998-IB961		19980622	
			20000217	PCT 371 date

	NUMBER	DATE
PRIORITY INFORMATION:	HU 1997-1081	19970623
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Goldberg, Jerome D.	
LEGAL REPRESENTATIVE:	Birch, Stewart, Kolasch & Birch, LLP	
NUMBER OF CLAIMS:	10	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	3 Drawing Figure(s); 3 Drawing Page(s)	
LINE COUNT:	751	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Pharmaceutical compositions having enhanced antitumor activity or reduced side effects. The compositions include both (A) a known active substance having antitumor effect or a pharmaceutically suitable salt thereof and (B) an effective amount of a hydroximic acid derivative of formula (I) ##STR1##

or a therapeutically useful acid addition salt thereof. Also disclosed are methods for reducing side effects in patients requiring treatment for tumors.

IT **66611-37-8 66611-38-9**
(hydroximic acid deriv.-antitumor agent pharmaceutical compn. with enhanced antitumor activity and/or reduced side effects)

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FILE COVERS 1907 - 9 Jul 2003  VOL 139 ISS 2
FILE LAST UPDATED: 8 Jul 2003  (20030708/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> d que nos l23; d que nos l27; d que nos l30

L7              STR
L9            6 SEA FILE=REGISTRY FAM FUL L7
L11          23 SEA FILE=HCAPLUS ABB=ON  L9
L12      275914 SEA FILE=HCAPLUS ABB=ON  ANTITUMOR AGENTS+OLD,NT,RTCS/CT
L13       13187 SEA FILE=HCAPLUS ABB=ON  CYTOPROTECTIVE AGENTS/CT
L14       27858 SEA FILE=HCAPLUS ABB=ON  DRUG INTERACTIONS+OLD,NT/CT
L15       67891 SEA FILE=HCAPLUS ABB=ON  TOXICITY+NT/CT
L16       10083 SEA FILE=HCAPLUS ABB=ON  CYTOTOXICITY+OLD/CT
L17       14612 SEA FILE=HCAPLUS ABB=ON  (SIDE OR ADVERSE)(L)(EFFECT# OR
                EVENT# OR REACTION#)/OBI
L22      276648 SEA FILE=HCAPLUS ABB=ON  NEOPLASM#/CW
L23           5 SEA FILE=HCAPLUS ABB=ON  L11 AND (L12 OR L22) AND (L13 OR L14
                OR L15 OR L16 OR L17)


L7              STR
L9            6 SEA FILE=REGISTRY FAM FUL L7
L11          23 SEA FILE=HCAPLUS ABB=ON  L9
L12      275914 SEA FILE=HCAPLUS ABB=ON  ANTITUMOR AGENTS+OLD,NT,RTCS/CT
L22      276648 SEA FILE=HCAPLUS ABB=ON  NEOPLASM#/CW
L26      394192 SEA FILE=HCAPLUS ABB=ON  ADV/RL
L27           4 SEA FILE=HCAPLUS ABB=ON  L11 AND (L12 OR L22) AND L26


L7              STR
L9            6 SEA FILE=REGISTRY FAM FUL L7
L11          23 SEA FILE=HCAPLUS ABB=ON  L9
L12      275914 SEA FILE=HCAPLUS ABB=ON  ANTITUMOR AGENTS+OLD,NT,RTCS/CT
L22      276648 SEA FILE=HCAPLUS ABB=ON  NEOPLASM#/CW
L29      172884 SEA FILE=HCAPLUS ABB=ON  PROTECT?/OBI
L30           4 SEA FILE=HCAPLUS ABB=ON  L11 AND (L12 OR L22) AND L29

=> s (123 or 127 or 130) not 119
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L59 1 (L23 OR L27 OR L30) NOT L19

=> fil toxcenter; d que nos 139; s 139 not 134

FILE 'TOXCENTER' ENTERED AT 13:14:07 ON 09 JUL 2003
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FILE COVERS 1907 TO 8 Jul 2003 (20030708/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

TOXCENTER has been enhanced with new files segments and search fields. See HELP CONTENT for more information.

TOXCENTER thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2003 vocabulary. See http://www.nlm.nih.gov/mesh/summ2003.html for a description on changes.

L7		STR
L9	6	SEA FILE=REGISTRY FAM FUL L7
L32	8	SEA FILE=TOXCENTER ABB=ON L9
L35	437038	SEA FILE=TOXCENTER ABB=ON ?TUMOR?
L36	585637	SEA FILE=TOXCENTER ABB=ON ?NEOPLAS? OR ?CANCER?
L37	2028127	SEA FILE=TOXCENTER ABB=ON ?PROTECT? OR ?TOXIC? OR ?DAMAG?
L38	687439	SEA FILE=TOXCENTER ABB=ON (SIDE OR ADVERSE)(L)(EFFECT# OR EVENT# OR REACTION#)
L39	6	SEA FILE=TOXCENTER ABB=ON L32 AND (L35 OR L36) AND (L37 OR L38)

L60 0 L39 NOT L34

=> fil uspatf; d que nos 150; s 150 not 149

FILE 'USPATFULL' ENTERED AT 13:14:07 ON 09 JUL 2003
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FILE COVERS 1971 TO PATENT PUBLICATION DATE: 8 Jul 2003 (20030708/PD)
FILE LAST UPDATED: 8 Jul 2003 (20030708/ED)
HIGHEST GRANTED PATENT NUMBER: US6591423
HIGHEST APPLICATION PUBLICATION NUMBER: US2003126664
CA INDEXING IS CURRENT THROUGH 8 Jul 2003 (20030708/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 8 Jul 2003 (20030708/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2003
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2003

>>> USPAT2 is now available. USPATFULL contains full text of the <<<
>>> original, i.e., the earliest published granted patents or <<<
>>> applications. USPAT2 contains full text of the latest US <<<
>>> publications, starting in 2001, for the inventions covered in <<<
>>> USPATFULL. A USPATFULL record contains not only the original <<<
>>> published document but also a list of any subsequent <<<
>>> publications. The publication number, patent kind code, and <<<
>>> publication date for all the US publications for an invention <<<
>>> are displayed in the PI (Patent Information) field of USPATFULL <<<
>>> records and may be searched in standard search fields, e.g., /PN, <<<
>>> /PK, etc. <<<

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L7              STR
L9            6 SEA FILE=REGISTRY FAM FUL L7
L40          15 SEA FILE=USPATFULL ABB=ON  L9
L42       65625 SEA FILE=USPATFULL ABB=ON  ?TUMOR?
L43       77923 SEA FILE=USPATFULL ABB=ON  ?NEOPLAS? OR ?CANCER?
L44     1263844 SEA FILE=USPATFULL ABB=ON  ?PROTECT? OR ?TOXIC? OR ?DAMAG?
L45       27749 SEA FILE=USPATFULL ABB=ON  (TUMOR OR ANTITUMOR OR NEOPLAS? OR
                ANTINEOPLAS? OR CANCER? OR ANTICANCER?)/IT
L46       18545 SEA FILE=USPATFULL ABB=ON  (PROTECT? OR CYTOPROTECT? OR TOXIC?
                OR NEPHROTOXIC? OR NEUROTOXIC? OR CYTOTOXIC? OR DAMAG?)/IT
L47         577 SEA FILE=USPATFULL ABB=ON  ((SIDE OR ADVERSE)(L)(EFFECT# OR
                EVENT# OR REACTION#))/IT
L48      176163 SEA FILE=USPATFULL ABB=ON  ((SIDE OR ADVERSE)(2A)(EFFECT# OR
                EVENT# OR REACTION#))
L50           6 SEA FILE=USPATFULL ABB=ON  L40 AND (L42 OR L43 OR L45) AND
                (L44 OR (L46 OR L47 OR L48))


L61           2 L50 NOT (L49 /
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=> d que l57

L51          55 SEA BGP15 OR BGP15M OR BGP(W)(15 OR 15M) OR NP51 OR NP 51
L52     6210971 SEA CANCER? OR TUMOR? OR TUMOUR? OR NEOPLAS?
L53      839168 SEA ANTICANCER? OR ANTITUMOR? OR ANTITUMOUR? OR ANTINEOPLAS?
L54     2026290 SEA (SIDE OR ADVERSE)(2A)(EFFECT# OR EVENT# OR REACTION#)
L55     5095799 SEA PROTECT? OR CYTOPROTECT? OR TOXIC? OR NEPHROTOXIC? OR
                NEUROTOXIC? OR CYTOTOXIC? OR DAMAG?
L56      787554 SEA CHEMOTHERAP?
L57          20 SEA L51 AND (L52 OR L53 OR L56) AND (L54 OR L55)


=> dup rem l57,l59,l60,l61
L60 HAS NO ANSWERS
FILE 'MEDLINE' ENTERED AT 13:15:05 ON 09 JUL 2003

FILE 'CANCERLIT' ENTERED AT 13:15:05 ON 09 JUL 2003

FILE 'DRUGU' ENTERED AT 13:15:05 ON 09 JUL 2003
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FILE 'BIOSIS' ENTERED AT 13:15:05 ON 09 JUL 2003
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FILE 'EMBASE' ENTERED AT 13:15:05 ON 09 JUL 2003
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FILE 'SCISEARCH' ENTERED AT 13:15:05 ON 09 JUL 2003
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FILE 'HCAPLUS' ENTERED AT 13:15:05 ON 09 JUL 2003
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FILE 'USPATFULL' ENTERED AT 13:15:05 ON 09 JUL 2003
CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)
PROCESSING COMPLETED FOR L57
PROCESSING COMPLETED FOR L59
PROCESSING COMPLETED FOR L60
PROCESSING COMPLETED FOR L61
L62          13 DUP REM L57 L59 L60 L61 (10 DUPLICATES REMOVED)
                ANSWERS '1-3' FROM FILE MEDLINE
                ANSWERS '4-7' FROM FILE DRUGU
                ANSWER '8' FROM FILE BIOSIS
                ANSWERS '9-10' FROM FILE EMBASE
                ANSWER '11' FROM FILE HCAPLUS
                ANSWERS '12-13' FROM FILE USPATFULL

=> d ibib ab 1-10; d ibib ab hitrn 11-13; fil hom

L62  ANSWER 1 OF 13     MEDLINE                              DUPLICATE 1
ACCESSION NUMBER:    2002199136     MEDLINE
DOCUMENT NUMBER:     21929391   PubMed ID: 11931842
TITLE:               BGP-15 - a novel poly(ADP-ribose)
                     polymerase inhibitor - protects against
                     nephrotoxicity of cisplatin without compromising
                     its antitumor activity.
AUTHOR:              Racz Ildiko; Tory Kalman; Gallyas Ferenc Jr; Berente
                     Zoltan; Osz Erzsebet; Jaszlits Laszlo; Bernath Sandor;
```

	Sumegi Balazs; Rabloczky Gyorgy; Literati-Nagy Peter
CORPORATE SOURCE:	N-Gene R&D, Szent Istvan Krt. 18, Budapest, Hungary.
SOURCE:	BIOCHEMICAL PHARMACOLOGY, (2002 Mar 15) 63 (6) 1099-111. Journal code: 0101032. ISSN: 0006-2952.
PUB. COUNTRY:	England: United Kingdom
DOCUMENT TYPE:	Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:	English
FILE SEGMENT:	Priority Journals
ENTRY MONTH:	200206
ENTRY DATE:	Entered STN: 20020405
	Last Updated on STN: 20020611
	Entered Medline: 20020610

AB **Nephrotoxicity** is one of the major dose limiting **side effects** of cisplatin **chemotherapy**. The **antitumor** and **toxic** effects are mediated in part by different mechanisms, thus, permitting a selective inhibition of certain **side effects**. The influence of O-(3-piperidino-2-hydroxy-1-propyl)nicotinic amidoxime (**BGP-15**) - a poly(ADP-ribose) polymerase (PARP) inhibitor - on the **nephrotoxicity** and **antitumor** efficacy of cisplatin has been evaluated in experimental models. **BGP-15** either blocked or significantly reduced (60-90% in 100-200 mg/kg oral dose) cisplatin induced increase in serum urea and creatinine level in mice and rats and prevented the structural degeneration of the kidney, as well. The nephroprotective effect of **BGP-15** treatment was revealed also in living mice by MRI analysis manifesting in the lack of oedema which otherwise developed as a result of cisplatin treatment. The **protective** effect was accompanied by inhibition of cisplatin-induced poly-ADP-ribosylation and by the restoration of the disturbed energy metabolism. The preservation of ATP level in the kidney was demonstrated in vivo by localized NMR spectroscopy. **BGP-15** decreased cisplatin-induced ROS production in rat kidney mitochondria and improved the antioxidant status of the kidney in mice with cisplatin-induced nephropathy. In rat kidney, cisplatin caused a decrease in the level of Bcl-x, a mitochondrial **protective** protein, and this was normalized by **BGP-15** treatment. On the other hand, **BGP-15** did not inhibit the **antitumor** efficacy of cisplatin in cell culture and in transplantable solid **tumors** of mice. Treatment with **BGP-15** increased the mean survival time of cisplatin-treated P-388 leukemia bearing mice from 13 to 19 days. PARP inhibitors have been demonstrated to diminish the consequences of free radical-induced **damage**, and this is related to the chemoprotective effect of **BGP-15**, a novel PARP inhibitor. Based on these results, we propose that **BGP-15** represents a novel, non-thiol chemoprotective agent.

L62 ANSWER 2 OF 13 MEDLINE DUPLICATE 2

ACCESSION NUMBER:	2002179257 MEDLINE
DOCUMENT NUMBER:	21909216 PubMed ID: 11911844
TITLE:	Reduction of acute photodamage in skin by topical application of a novel PARP inhibitor.
AUTHOR:	Farkas Beatrix; Magyarlaki Marta; Csete Bela; Nemeth Jozsef; Rabloczky Gyorgy; Bernath Sandor; Literati Nagy Peter; Sumegi Balazs
CORPORATE SOURCE:	Department of Dermatology, Faculty of Medicine; University of Pecs, Kodaly u. 20, H-7624, Pecs, Hungary.. farkasb@derma.pote.hu
SOURCE:	BIOCHEMICAL PHARMACOLOGY, (2002 Mar 1) 63 (5) 921-32. Journal code: 0101032. ISSN: 0006-2952.
PUB. COUNTRY:	England: United Kingdom
DOCUMENT TYPE:	Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:	English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 20020326
Last Updated on STN: 20020508
Entered Medline: 20020507

AB The ultraviolet (UV) components of sunlight induce **damage** to the DNA in skin cells, which is considered to be the initiating step in the harmful biological effects of UV radiation. Repair of DNA **damage** results in the formation of single-strand DNA breaks, which activate the nuclear poly(ADP-ribose) polymerase (PARP). Overactivation of PARP worsens the oxidative cell **damage** and impairs the energy metabolism, raising the possibility that moderation of PARP activation following DNA **damage** may **protect** skin cells from UV radiation. The topical effects of the novel PARP inhibitor O-(3-pyperidino-2-hydroxy-1-propyl) pyridine-3-carboxylic acid amidoxime monohydrochloride (**BGP-15M**) were investigated on UV-induced skin **damage** in a hairless mouse model. For evaluation of the UV-induced acute photodamage to the skin and the potential **protective** effect of **BGP-15M**, DNA injury was detected by measuring the formation of single-strand DNA breaks and counting the resulting sunburn (apoptotic) cells. The ADP-ribosylation of PARP was assessed by Western blot analysis and then quantified. In addition, the UV-induced immunosuppression was investigated by the immunostaining of **tumor** necrosis factor alpha and interleukin-10 expressions in epidermal cells. The signs of inflammation were examined clinically and histochemically. Besides its primary effect in decreasing the activity of nuclear PARP, topically applied **BGP-15M** proved to be **protective** against solar and artificial UV radiation-induced acute skin **damage**. The DNA injury was decreased ($P<0.01$). An inhibition of immunosuppression was observed by down-regulation of the epidermal production of cytokines IL-10 and TNFalpha. In the mouse skin, clinical or histological signs of UV-induced inflammation could not be observed. These data suggest that **BGP-15M** directly interferes with UV-induced cellular processes and modifies the activity of PARP. The effects provided by topical application of the new PARP-regulator **BGP-15M** indicate that it may be a novel type of agent in photoprotection of the skin.

L62 ANSWER 3 OF 13 MEDLINE
ACCESSION NUMBER: 2003305336 IN-PROCESS
DOCUMENT NUMBER: 22717394 PubMed ID: 12831778
TITLE: **BGP-15**, a hydroximic acid derivative, **protects** against cisplatin- or taxol-induced peripheral neuropathy in rats.
AUTHOR: Bardos G; Moricz K; Jaszlits L; Rabloczky G; Tory K; Racz I; Bernath S; Sumegi B; Farkas B; Literati-Nagy B; Literati-Nagy P
CORPORATE SOURCE: Department of Physiology and Neurobiology, Eotvos Lorand University, Budapest, Hungary.
SOURCE: TOXICOLOGY AND APPLIED PHARMACOLOGY, (2003 Jul 1) 190 (1) 9-16.
Journal code: 0416575. ISSN: 0041-008X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20030701
Last Updated on STN: 20030701

AB The neuroprotective effect of **BGP-15** against peripheral sensory neuropathy was studied in rats that were exposed to short-term cisplatin or taxol administration. The changes of nerve conduction velocity were determined in situ after treating the Wistar rats

with **BGP-15** (50, 100, and 200 mg/kg po daily doses throughout the experiment), cisplatin (1.5 mg/kg ip daily dose for 5 days), or taxol (5.0 mg/kg ip daily dose every other day in a 10-day interval) alone or giving the test compound in combination with cisplatin or taxol. Electrophysiological recordings were carried out in vivo by stimulating the sciatic nerve at both sciatic notch and ankle site. Neither motor nor sensory nerve conduction velocity was altered by any dose level of **BGP-15** tested. Both **anticancer** drugs decreased the sensory nerve conduction velocity (SNCV). **BGP -15** treatment prevented the impairment of SNCV either in part or totally in the cisplatin- or taxol-treated groups. This neuroprotective potential of **BGP-15** could be well correlated with its recently described poly(ADP-ribose) polymerase- inhibitory effect and its ability to **protect** against the **damages** induced by the increased level of reactive oxygen species in response to **anticancer** treatment.

L62 ANSWER 4 OF 13 DRUGU COPYRIGHT 2003 THOMSON DERWENTDUPLICATE 3
ACCESSION NUMBER: 2002-03080 DRUGU B P S
TITLE: Mode of action observations of a new chemoprotective agent **BGP-15**.
AUTHOR: Tory K; Racz I; Gallyas F; Jaszlits L; Bernath S; Sumegi B; Rabloczky G; Literati Nagy P
CORPORATE SOURCE: Univ.Pecs; N-Gene
LOCATION: Pecs; Budapest, Hung.
SOURCE: Proc.Am.Assoc.Cancer Res. (42, 92 Meet., 512, 2001) ISSN: 0197-016X
AVAIL. OF DOC.: Department of Biochemistry, University of Pecs, Faculty of Medicine Pecs, Pecs, Hungary.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB The mechanism of the chemoprotective effect of **BGP-15** (O-(3-piperidino 2-hydroxy 1-propyl) nicotinic amidoxime) was studied in vitro. **BGP-15** decreased cisplatin-induced free radical formation in isolated rat kidney mitochondria. In addition, **BGP-15** restored the decreased Bcl-X level in cisplatin-induced **nephrotoxicity**, and the decreased glutathione level and catalase activity, while it had no effect on SOD activity. Increased free radical formation contributes to the **side-effects** of **antitumor** agents. The data show that **BGP-15** exerts its **protective** effect, at least in part, by decreasing the formation of free radicals. (conference abstract: 92nd Annual Meeting of the American Association for **Cancer** Research, New Orleans, Louisiana, USA, 2001).

L62 ANSWER 5 OF 13 DRUGU COPYRIGHT 2003 THOMSON DERWENT
ACCESSION NUMBER: 2002-42166 DRUGU B P
TITLE: Beneficial effect of poly(ADP-ribose) polymerase (PARP) inhibitor in acute photodamage.
AUTHOR: Farkas B; Csete B; Magyarlaki M; Nemeth J; Tubak V; Literati Nagy P; Sumegi B
LOCATION: Pecs; Budapest, Hung.
SOURCE: J.Invest.Dermatol. (119, No. 3, 740, 2002)
CODEN: JIDEAE ISSN: 0022-202X
AVAIL. OF DOC.: No Reprint Address.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB The effects of topical **BGP-15M** on acute UV-induced skin **damage** were studied in hairless mice. **BGP-**

15M (BGP-15) reduced nuclear poly(ADP-ribose) polymerase (PARP) activity, DNA **damage** and apoptosis, down-regulated epidermal IL-10 and TNF-alpha production, and prevented inflammation. The results suggest that **BGP-15M** may be a novel type of photoprotective agent. (conference abstract: 32nd Annual European Society for Dermatological Research (ESDR) Meeting, Geneva, 2002). (No EX).

L62 ANSWER 6 OF 13 DRUGU COPYRIGHT 2003 THOMSON DERWENT
ACCESSION NUMBER: 2000-30219 DRUGU P S
TITLE: A novel chemoprotective compound with poly(ADP-ribose)polymerase inhibitor activity.
AUTHOR: Tory K; Racz I; Gal D; Jaszlits L; Rabloczky G; Bernath S; Sumegi B; Literati Nagy P
CORPORATE SOURCE: Univ.Med.Pecs; N-Gene; Nat.Inst.Oncol.Budapest
LOCATION: Pecs; Budapest, Hung.
SOURCE: Proc.Am.Assoc.Cancer Res. (41, 91 Meet., 201, 2000) ISSN: 0197-016X
AVAIL. OF DOC.: Medical University, Pecs, Hungary.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB The use of **BGP-15** to **protect** against the **toxicity** of cisplatin was studied in mice and rats. **BGP-15 protected** against lethality, **neurotoxicity** and **nephrotoxicity**, in-vivo and in-vitro, without affecting the **antitumor** efficacy of cisplatin. The most likely mechanism is considered to be inhibition of excessive poly(ADP-ribose) polymerase activation. (conference abstract: 91st Annual Meeting of the American Association for **Cancer** Research, San Francisco, California, USA, 2000).

L62 ANSWER 7 OF 13 DRUGU COPYRIGHT 2003 THOMSON DERWENT
ACCESSION NUMBER: 2001-24416 DRUGU B P
TITLE: Inhibition of nuclear poly(ADP-ribose)polymerase **protects** the kidney from **cytotoxic damage**.
AUTHOR: Racz I B; Tory K; Jaszlits L; Rabloczky G; Bernath S; Sumegi B; Literati-Nagy P
CORPORATE SOURCE: Univ.Pecs
LOCATION: Budapest; Pecs, Hung.
SOURCE: J.Physiol.(London) (526, Suppl. Proc., 178P-179P, 2000) CODEN: JPHYA7 ISSN: 0022-3751
AVAIL. OF DOC.: N-GENE R&D, Budapest, Hungary.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB The aim of the study was to determine whether p.o. **BGP-15**, which has poly(ADP-ribose)polymerase (PARP) inhibitor activity, can **protect** in-vivo against the **toxic side-effect (nephrotoxicity)** of the **antitumor** agent cisplatin (i.p.). **BGP-15** was able to diminish the DNA **damaging** effect of free radicals, excessively generated under pathological conditions, via a partial inhibition of PARP, a nuclear enzyme. (conference abstract: Scientific Meeting of the Physiological Society, Budapest, Hungary, 2000).

L62 ANSWER 8 OF 13 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:529158 BIOSIS
DOCUMENT NUMBER: PREV200000529158
TITLE: Inhibition of nuclear poly(ADP-ribose) polymerase

protects the kidney from **cytotoxic damage.**

AUTHOR(S): Racs, I. B. (1); Tory, K. (1); Jaszlits, L. (1); Rabloczky, G. (1); Bernath, S. (1); Sumegi, B.; Literati-Nagy, P. (1)

CORPORATE SOURCE: (1) N-Gene R and D, Budapest Hungary

SOURCE: Journal of Physiology (Cambridge), (August, 2000) Vol. 526P, pp. 178P-179P. print.
Meeting Info.: Scientific Meeting of the Physiological Society Budapest, Hungary May 27-29, 2000 Physiological Society
. ISSN: 0022-3751.

DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L62 ANSWER 9 OF 13 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001121590 EMBASE
TITLE: Molecular targets for pharmacological **cytoprotection.**
AUTHOR: Balla A.; Toth B.; Timar G.; Bak J.; Krajcsi P.
CORPORATE SOURCE: P. Krajcsi, Department of Medical Biochemistry, Semmelweis University, VIII. Puskin st. 9, H-1444 Budapest, Hungary. Krajcsi@puskin.sote.hu
SOURCE: Biochemical Pharmacology, (1 Apr 2001) 61/7 (769-777).
Refs: 100
ISSN: 0006-2952 CODEN: BCPCA6
PUBLISHER IDENT.: S 0006-2952(00)00585-2
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Cell death is common to many pathological conditions. In the past two decades, research into the mechanism of cell death has characterized the cardinal features of apoptosis and necrosis, the two distinct forms of cell death. Studies using in vivo disease models have provided evidence that apoptosis is induced by an array of pathological stimuli. Thus, molecular components of the machinery of apoptosis are potential pharmacological targets. The mechanism of apoptosis can be dissected into: (i) the initiation and signaling phase, (ii) the signal amplification phase, and (iii) the execution phase. Reflecting on the diversity of apoptotic stimuli, the initiation and signaling phase utilizes a variety of molecules: free radicals, ions, plasma membrane receptors, members of the signaling kinase cascades, transcription factors, and signaling caspases. In most of the apoptotic scenarios, impairment of mitochondrial function is an early event. Dysfunctioning mitochondria release more free radicals and hydrolytic enzymes (proteases and nucleases), amplifying the primary death signal. In the final phase of apoptosis, executioner caspases are activated. Substrates of the executioner caspases include nucleases, members of the cellular repair apparatus, and cytoskeletal proteins. Partial proteolysis of these substrates leads to distinctive morphological and biochemical changes, the hallmarks of apoptosis. The first steps toward pharmacological utilization of specific modifiers of apoptosis have been promising. However, since the potential molecular targets of **cytoprotective** therapy play important roles in the maintenance of cellular homeostasis, specificity (diseased versus healthy tissue) of pharmacological modulation is the key to success. .COPYRGT. 2001 Elsevier Science Inc.

L62 ANSWER 10 OF 13 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 1999315273 EMBASE
TITLE: A novel PARP inhibitor, ion channel modulation and AD therapies.
AUTHOR: Worker C.
CORPORATE SOURCE: C. Worker, Current Drugs Ltd, Middlesex House, 34-42 Cleveland Street, London W1P 6LB, United Kingdom. charlotte@cursci.co.uk
SOURCE: IDrugs, (1999) 2/9 (859-860).
ISSN: 1369-7056 CODEN: IDRUFN
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 037 Drug Literature Index
030 Pharmacology
038 Adverse Reactions Titles
018 Cardiovascular Diseases and Cardiovascular Surgery
LANGUAGE: English
SUMMARY LANGUAGE: English

AB On the fourth and final day of the EPHAR congress, ion channel modulation was the topic for two symposia and plenary lectures. The potential of dual potassium and calcium channel blockers as antiarrhythmics was discussed, amongst other applications for ion channel modifiers. Several presentations were dedicated to the disclosure of a novel PARP inhibitor, **BGP-15**, developed at the University Medical School of Pecs in Hungary. This compound is emerging as a promising potential anti-ischemic and a chemoprotective agent. The treatment of Alzheimer's disease (AD) was the subject of further discussions; a detailed presentation was given by a psychiatrist from the US, describing the treatment regimens favored in her clinic, as well as a complete review of currently available and potentially new AD therapies.

L62 ANSWER 11 OF 13 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:436213 HCAPLUS
DOCUMENT NUMBER: 127:55919
TITLE: Hydroxylamine derivatives useful for enhancing molecular chaperon production and the preparation thereof
INVENTOR(S): Vigh, Laszlo; Literati Nagy, Peter; Szilbereky, Jeno; Uerogdi, Laszlo; Jednakovits, Andrea; Jaszlits, Laszlo; Biro, Katalin; Marvanyos, Ede; Barabas, Mihaly; Hegedues, Erzsebet; Koranyi, Laszlo; Kuerthy, Maria; Balogh, Gabor; Horvath, Ibolya; Torok, Zsolt; Udvardy, Eva; Dorman, Gyorgy; Medzihradszky, Denes; Mezes, Bea; Kovacs, Eszter; Duda, Erno; Farkas, Beatrix; Glatz, Attila; et al.
PATENT ASSIGNEE(S): Hung.
SOURCE: PCT Int. Appl., 179 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9716439	A1	19970509	WO 1996-HU64	19961101
W: AU, BG, BR, CA, CN, CZ, IL, JP, KR, LT, LV, MX, NO, NZ, PL, RO, RU, SK, UA, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
HU 76659	A2	19971028	HU 1995-3141	19951102
CA 2209167	AA	19970509	CA 1996-2209167	19961101

AU 9673263	A1	19970522	AU 1996-73263	19961101
AU 720195	B2	20000525		
EP 801649	A2	19971022	EP 1996-935195	19961101
EP 801649	B1	20020807		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CN 1177351	A	19980325	CN 1996-192305	19961101
BR 9607565	A	19990720	BR 1996-7565	19961101
AT 221880	E	20020815	AT 1996-935195	19961101
ES 2176502	T3	20021201	ES 1996-935195	19961101
NO 9703059	A	19970902	NO 1997-3059	19970701

PRIORITY APPLN. INFO.: HU 1995-3141 A 19951102
HU 1996-3919 A 19960209
HU 1996-29820 A 19961004
WO 1996-HU64 W 19961101
WO 1996-HU664 19961101

OTHER SOURCE(S): MARPAT 127:55919

AB A method of increasing expression of a mol. chaperon by a cell and/or enhancing the activity of a mol. chaperon in cells is provided. The method comprises treating a cell that is exposed to a physiol. stress which induces expression of a mol. chaperon by the cell with an effective amt. of a certain hydroxylamine deriv. to increase the stress. Alternatively, a hydroxylamine deriv. can be administrated to a cell before it is exposed to a physiol. stress which induces expression of a mol. chaperon by the cell. Preferably, the cell to which a hydroxylamine deriv. is administered is a eukaryotic cell. The invention also provides novel hydroxylamine derivs. falling within the scope of the formulas AZC(X):NOR (A = alkyl, substituted alkyl, aralkyl, substituted aralkyl, heteroaryl, etc.; Z = covalent bond, O, or NR3, where R3 = H, alkyl, substituted alkyl, aryl, etc.; R = alkyl or substituted alkyl; X = halo, substituted hydroxy or amino, substituted amino; R' = H, alkyl, substituted alkyl, aryl, substituted aryl, etc.) and AZC(:X)N(R')OR (A = alkyl, substituted alkyl, aralkyl, substituted aralkyl, heteroaryl, etc.; Z = covalent bond, O, or NR3, where R3 = H, alkyl, substituted alkyl, aryl, etc.; R = alkyl or substituted alkyl; X =O, imino, or substituted imino; R' = H, alkyl, substituted alkyl, aryl, substituted aryl, etc.) as well as pharmaceutical and/or cosmetic compns. comprising the said compds.

IT **66611-38-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(hydroxylamine derivs. useful for enhancing mol. chaperon prodn. and the prepn. thereof)

L62 ANSWER 12 OF 13 USPATFULL

ACCESSION NUMBER: 2002:242758 USPATFULL

TITLE: Method for treating the pathological lesions of the skin that develop by ultraviolet radiation of the sunlight

INVENTOR(S): Farkas, Bea, Szeged, HUNGARY
Nagy, Peter Literati, Budapest, HUNGARY
Vadasz, Agnes, Budapest, HUNGARY
Vigh, Laszlo, Szeged, HUNGARY

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002131938	A1	20020919
APPLICATION INFO.:	US 2001-5074	A1	20011207 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1998-205281, filed on 4 Dec 1998, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	HU 1995-P3728	19951222

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BIRCH STEWART KOLASCH & BIRCH, PO BOX 747, FALLS CHURCH, VA, 22040-0747
NUMBER OF CLAIMS: 14
EXEMPLARY CLAIM: 1
LINE COUNT: 451
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to methods for prevention and/or treatment of skin lesions caused by exposure to ultraviolet radiation. Exemplary condition that can be prevented or treated are actinic keratosis, dry skin, polymorphic light exanthema, photopathology, photo-allergy, solar atrophy, stria migrans, elastoma diffusum, X-ray dermatits, gouty polychondritis and decubitis ulcer. The method employs application to the skin of a composition comprising a hydroximic acid derivative of the formula ##STR1##

IT **66611-38-9 459809-32-6**
(nicotinic amidoxime deriv. compns. for treating pathol. lesions of the skin that develop by UV radiation of the sunlight)

L62 ANSWER 13 OF 13 USPATFULL
ACCESSION NUMBER: 2002:254060 USPATFULL
TITLE: Cosmetic composition and a method for the prevention and/or reduction of the photoaging processes of the skin
INVENTOR(S): Farkas, Bea, Szeged, HUNGARY
Nagy, Peter Literati, Budapest, HUNGARY
Vadasz, Agnes, Budapest, HUNGARY
Vigh, Laszlo, Szeged, HUNGARY
PATENT ASSIGNEE(S): Medgene, Limited, Tortola, VIRGIN ISLANDS (BRITISH) (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6458371	B1	20021001
APPLICATION INFO.:	US 1998-205281		19981204 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1996-771410, filed on 20 Dec 1996, now abandoned

	NUMBER	DATE
PRIORITY INFORMATION:	HU 1995-3728	19951222

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Hartley, Michael G.
ASSISTANT EXAMINER: Willis, Michael A.
LEGAL REPRESENTATIVE: Birch Stewart Kolasch & Birch LLP
NUMBER OF CLAIMS: 18
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 507
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A novel cosmetic composition comprising a known hydroximic acid derivative as the active ingredient, and conventional carriers of the cosmetic composition are disclosed. The cosmetic composition of the invention is suitable for the prevention and/or reduction of the photoaging processes of the skin exposed to UV radiation.

IT **66611-38-9**
(cosmetic compn. contg. hydroximic acid deriv. for prevention and redn. of skin photoaging)

FILE 'HOME' ENTERED AT 13:15:55 ON 09 JUL 2003